

**PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of )  
Kornelia Polyak, *et al.* ) Examiner: TBA  
Serial No. TBA ) Group Art Unit: TBA  
Filed: January 24, 2002 ) Atty. Dkt. No. 001107.00224

For: **SUBTLE MITOCHONDRIAL MUTATIONS AS TUMOR MARKERS**

**PRELIMINARY AMENDMENT**

The Honorable Assistant Commissioner for  
Patents  
Washington, D.C. 20231

Sir:

Please enter the following amendment prior to examination on the merits. It is believed that no fee is required to enter this amendment. If any fees are required for entry and consideration of this amendment, please charge our deposit account no. 19-0733.

**IN THE SPECIFICATION**

Please substitute the following as the first paragraph of the specification, immediately after the title.

This application claims the priority of provisional U.S. Application Ser. No. 60/097,307, filed August 20, 1998, and is a continuation of U.S. Application Ser. No. 09/377,856, filed August 20, 1999.

## IN THE CLAIMS

Please cancel claims 17-28.

Please amend claims 1, 2, 9-11, 30 and 31 to read as follows.

1. A method to aid in detecting the presence of tumor cells in a patient, comprising the steps of:

determining the presence of a single basepair mutation in a mitochondrial genome of a cell sample of a patient, wherein the mutation is found in a tumor of the patient but not in normal tissue of the patient; and

identifying the patient as having a tumor if one or more single basepair mutations are determined in the mitochondrial genome of the cell sample of the patient.

2. The method of claim 1 wherein, prior to the determining, the mutation has been identified in a tumor.

9. The method of claim 1 wherein the step of determining comprises amplifying mitochondrial DNA.

10. The method of claim 1 wherein the step of determining comprises sequencing mitochondrial DNA.

11. The method of claim 1 wherein the step of determining comprises hybridization of DNA amplified from the mitochondrial genome of the cell sample to an array of oligonucleotides which comprises matched and mismatched sequences to human mitochondrial genomic DNA.

30. The method of claim 29 wherein the patient has received anti-cancer therapy and the step of determining is performed at least three times to monitor progress of the anti-cancer therapy.

31. The method of claim 1 further comprising the step of testing a normal tissue of the patient to determine the absence of the mutation.

Please add the following new claim.

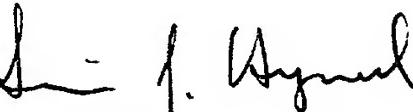
32. The method of claim 1 wherein the cell sample is from a tumor.

**REMARKS**

Claims 17-28 have been canceled because these claims were allowed in the parent case. The other claim amendments, including the addition of new claim 32, place the remaining claims in the same form as at the conclusion of prosecution in the parent case. The specification has been amended to add reference to the parent case. The amendments do not add new matter.

Claims 1-16 and 29-32 are being examined.

Respectfully submitted,

By:   
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Date: January 24, 2002

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## Marked-Up Copy of Claims and Specification Showing Amendments

### Amendments to Specification

This application claims the priority of provisional U.S. Application Ser. No. 60/097,307, filed August 20, 1998, and is a continuation of U.S. Application Ser. No. 09/377,856, filed August 20, 1999.

### Amendments to Claims

1. A method to aid in detecting the presence of tumor cells in a patient, comprising the steps of:

[step for] determining the presence of a single basepair mutation in a mitochondrial genome of a cell sample of a patient, wherein the mutation is found in a tumor of the patient but not in normal tissue of the patient; and

identifying the patient as having a tumor if one or more single basepair mutations are determined in the mitochondrial genome of the cell sample of the patient.

2. The method of claim 1 wherein, prior to the [step for] determining, the mutation has been identified in a tumor.

9. The method of claim 1 wherein the step of [for] determining comprises amplifying mitochondrial DNA.

10. The method of claim 1 wherein the step of [for] determining comprises sequencing mitochondrial DNA.

11. The method of claim 1 wherein the step of [for] determining comprises hybridization of DNA amplified from the mitochondrial genome of the cell sample to an array of oligonucleotides which comprises matched and mismatched sequences to human mitochondrial genomic DNA.

30. The method of claim 29 wherein the patient has received anti-cancer therapy and the step of [for] determining is performed at least three times to monitor progress of the anti-cancer therapy.

31. The method of claim 1 further comprising the [a] step of [for] testing a normal tissue of the patient to determine the absence of the mutation.